(11) M. K. Wolpert-DeFilippes, R. H. Adamson, R. L. Cysyk, and D. G. Johns, *Biochem. Pharmacol.*, **24**, 751 (1975).
(12) T. E. O'Connor, C. Aldrich, A. Hadidi, N. Lomex, P. Okano, S. Sethi, and H. B. Wood, *Proc. Am. Assoc. Cancer Res.*, **16**, Abstr. 114 (1975).
(13) M. K. Wolpert-DeFilippes, V. H. Bono, Jr., R. L. Dion, and D. G. Johns, *Biochem. Pharmacol.*, **24**, 1735 (1975).
(14) F. Mandelbaum-Shavit, M. K. Wolpert-DeFilippes, and D. G. Johns, *Biochem. Biophys. Res. Commun.*, **72**, 47 (1976).
(15) R. H. Adamson, S. M. Sieber, J. Whang-Peng, and H. B. Wood, *Proc. Am. Assoc. Cancer Res.*, **17**, Abstr. 165 (1976).
(16) C. D Aldrich and T. E. O'Connor, *Proc. Am. Assoc. Cancer Res.*, **17**, Abstr. 339 (1976).
(17) S. M. Sieber, M. K. Wolpert, R. H. Adamson, R. L. Cysyk, V. H. Bono, and D. G. Johns, *Bibl. Haematol. (Basel)*, *495* (1976); *Chem. Abstr.*, **85**, 104123p (1976).
(18) Pilot experiments indicated that treatment with acetic anhydride–pyridine facilitated the subsequent separation without affecting the active principles.
(19) K. Sesaki, K. L. Rinehart, Jr., G. Slomp, M. F. Grostic, and E. C. Olson, *J. Am. Chem. Soc.*, **92**, 7591 (1970).
(20) R. F. Bryan, C. J. Gilmore, and R. C. Haltiwanger, *J. Chem. Soc., Perkin Trans. 2*, 897 (1973).
(21) T. H. Siddall and W. E. Stewart, *Progr. Nucl. Magn. Reson. Spectrosc.*, **5**, 33 (1969).
(22) L. M. Jackman and S. Sternhill, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed, Pergamon Press, Elmsford, N.Y., 1969, p 368.
(23) H. Krebs and W. Schumacher, *Chem. Ber.*, **99**, 1341 (1966).
(24) W. Cole and P. L. Julian, *J. Org. Chem.*, **19**, 131 (1954).
(25) M. C. Wani, H. L. Taylor, and M. E. Wall, *J. Chem. Soc., Chem. Commun.*, 390 (1973).
(26) Stem wood and stem bark were collected in South Africa in 1972. We again acknowledge with thanks receipt of the dried plant material from Dr. Robert E. Perdue, Jr.
(27) Later collections of *P. verrucosa* have also been assayed for maytansine yield and have been found to average 8–9 mg/kg.
(28) We thank Professor a. I. Meyers, Colorado State University, for unpublished information concerning $LiAlH_4$ reductive cleavage of esters in synthetic model compounds.
(29) M. P. Mertes, P. E. Hanna, and A. A. Ramsey, *J. Med. Chem.*, **13**, 125 (1969).
(30) H. C. Brown, *J. Am. Chem. Soc.*, **60**, 1325 (1938).
(31) I. M. Kolthoff and C. Rosenblum, "Acid-Base Indicators", Macmillan, New York, N.Y., 1937, p 249.

Studies of Resin Acids. 10. Approaches to the Synthesis of Podocarpic and Dehydroabietic Acids†[1]

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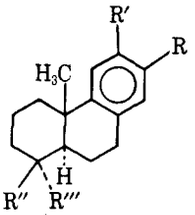
In a new stereoselective synthesis of the tricyclic nucleus of the resin acids, 2-(2-phenylethyl)cyclohexane-1,3-dione is cyclized to a tricyclic enone (**5**). Conjugate addition of lithium dimethylcuprate gives a mixture of the 5α and 5β isomers of 18,19-dinorpodocarpa-8,11,13-triene (**6**), which reacts with methylenetriphenylphosphorane to give as a major product olefin **7**, which is also prepared from podocarpic acid (**2**). A new stereoselective synthesis of dehydroabietic acid (**1**) from the dinorketone **9** via the sequence methylenetriphenylphosphorane to olefin **10**, conversion of **10** to aldehyde **17**, alkylation with allyl bromide to **22**, is presented. Wolff–Kishner reduction of **22** followed by oxidation affords homodehydroabietic acid (**24**), which has been converted previously to acid **1**.

Although a number of syntheses of diterpenoid acids, such as dehydroabietic acid (abieta-8,11,13-trien-18-oic acid, **1**) and podocarpic acid (12-hydroxypodocarpa-8,11,13-trien-19-oic acid, **2**) have been described,[3] all of these syntheses are rather lengthy and many are nonstereoselective. Also, in none of these syntheses could a single intermediate well along the synthetic route be used to obtain stereoselectively both epimeric C-4 carboxylic acids. Either the reaction sequence gave a mixture of epimers at this center, or the synthesis was designed in such a way that it provided only one epimer from the outset.

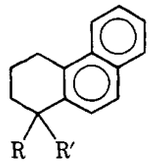
In an effort to overcome both of these shortcomings a new approach to the total synthesis of these diterpenoid acids has been devised which is a modification of an earlier synthesis, reported from this laboratory, which resulted in a short, stereoselective synthesis of eudesmol and several related sesquiterpenes.[4] The modified synthetic sequence as applied to the diterpene acids is shown in Scheme I. In order to utilize readily available starting materials, this approach was to be applied to the syntheses of podocarpa-8,11,13-trien-18-oic (**3**) and -19-oic (**4**) acids, both of which have been converted to naturally occurring compounds.[3e,5]

The key steps of the synthesis were first, the conjugate addition of lithium dimethylcuprate to enone **5**, and second, the reaction of methylenetriphenylphosphorane with ketone **6** to give selectively the 5α olefin (**7**). Olefin **7** could easily be transformed to aldehyde **8**, which then could, hopefully, be utilized to synthesize acids **3** and **4**.

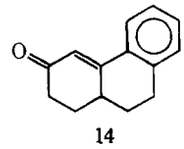
† Dedicated to Professor R. B. Woodward on the occasion of his 60th birthday.



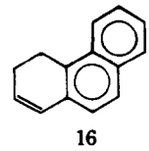
1, R = $CH(CH_3)_2$; R′ = H; R″ = CH_3; R‴ = CO_2H
2, R = H; R′ = OH; R″ = CO_2H; R‴ = CH_3
3, R,R′ = H; R″ = CH_3; R‴ = CO_2H
4, R,R′ = H; R″ = CO_2H; R‴ = CH_3
11, R = $CH(CH_3)_2$; R′,R‴ = H; R″ = CH_3
18, R = $CH(CH_3)_2$; R′ = H; R″ = CO_2H; R‴ = CH_3
20, R = $CH(CH_3)_2$; R′ = H; R″ = CHO; R‴ = CH_3
21, R = $CH(CH_3)_2$; R′ = H; R″,R‴ = CH_3
22, R = $CH(CH_3)_2$; R′ = H; R″ = CHO; R‴ = $CH_2CH{=}CH_2$
23, R = $CH(CH_3)_2$; R′ = H; R″ = CH_3; R‴ = $CH_2CH{=}CH_2$
24, R = $CH(CH_3)_2$; R′ = H; R″ = CH_3; R‴ = CH_2CO_2H



12, R,R′ = O
13, R,R′ = H
15, R = OH; R′ = H



14



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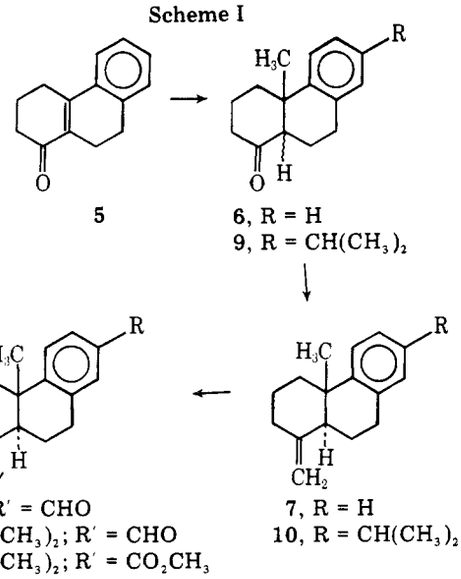
In order to ascertain the feasibility of the trans-selective Wittig reaction which had worked well in other cases,[4,6] the

Scheme I



5 6, R = H; 9, R = $CH(CH_3)_2$

8, R = H; R′ = CHO
17, R = $CH(CH_3)_2$; R′ = CHO
19, R = $CH(CH_3)_2$; R′ = CO_2CH_3

7, R = H
10, R = $CH(CH_3)_2$

model reaction of ketone **9**, readily obtainable as a mixture of 5α and 5β isomers by degradation of dehydroabietic acid,[7] with methylenetriphenylphosphorane was investigated. The preparation of ketone **9** was modified by first separating the precursor olefin (**10**) from the mixture of olefins obtained from the lead tetraacetate oxidation of dehydroabietic acid[8] by means of selective epoxidation[9] and then cleaving the olefin by oxidation with periodate–permanganate.

In contrast to earlier reports,[4,6] the Wittig reaction of ketone **9** with methylenetriphenylphosphorane under a variety of conditions was found not to be completely stereoselective with the product containing 90% of the desired 5α isomer (**10**). The structure and stereochemistry of the major product of the Wittig reaction were confirmed by hydrogenation to 18-norabieta-8,11,13-triene (**11**).[8] Based on spectral data, the balance of the hydrocarbon fraction was the undesired 5β isomer. Following the completion of this phase of the work, Ziegler reported the reaction of a very similar ketone with methoxymethylenetriphenylphosphorane to give the 5α isomer with unspecified stereoselectivity.[10]

The second key step in the synthesis was the conjugate addition of lithium dimethylcuprate[11] to tricyclic enone **5**. This enone had been prepared some years ago from 2-(2-phenylethyl)cyclohexane-1,3-dione on treatment with polyphosphoric acid.[12] Repetition of this synthesis, under conditions which apparently duplicated those published, gave a complex mixture of **5**, 1,2,3,4-tetrahydro-1-phenanthrone (**12**), phenanthrene, and 1,2,3,4-tetrahydrophenanthrene (**13**), apparently resulting from complex hydride transfer reactions.

In one reaction a small quantity of 1,2,3,9,10,10a-hexahydro-3-phenanthrone[13] (**14**) was obtained. This material is undoubtedly an artifact arising from the cyclization of 4-(2-phenylethyl)cyclohexane-1,3-dione present as a contaminent in the dione precursor to enone **5**.[14]

Some effort was made to ascertain the course of the hydride transfer reactions in these cyclization reactions of 2-(2-phenylethyl)cyclohexane-1,3-dione. From these experiments the following conclusions could be reached: (1) The use of purified 2-(2-phenylethyl)cyclohexane-1,3-dione almost completely suppressed the hydride transfer reactions. (2) Carrying out the cyclization under relatively dilute conditions suppressed the hydride transfer reactions. (3) Once formed, enone **5** is stable to hot polyphospheric acid. In addition, two probable intermediates in the hydride transfer reactions, 1,2,3,4-tetrahydro-1-phenanthrol[15] (**15**) and 3,4-dihydrophenanthrene (**16**), were prepared in order to investigate their possible role in this reaction.

Although 3,4-dihydrophenanthrene has been reported previously, in one case the compound was not characterized[16] and in the other[17] the physical properties did not agree with those of material prepared by the dehydration of alcohol **15**. In order to clarify this situation, olefin **16** was oxidized to the corresponding diacid, which was identical with a sample prepared from ketone 12,[18] thus confirming that our material had the assigned structure. Based on the published data, it appears that the dihydrophenanthrene reported by Paquette from the pyrolysis of "benzosnoutene"[17] is actually 1,2-dihydrophenanthrene.

Treatment of alcohol **15** or dihydrophenanthrene **16** with hot polyphosphoric acid gave low to modest yields of mixtures of phenanthrene and tetrahydrophenanthrene (**13**). While a mechanism can be proposed which accounts for most of these data, some points remain obscure.[19] It was finally found that by carrying out the cyclization under moderately dilute conditions, using purified diketone acceptable yields of recrystallized enone **5** could be obtained.

The conjugate addition of lithium dimethylcuprate to enone **5** gave a mixture of both isomers of **6**, which contained a preponderance (88%) of the 5β ketone. Isomerization of this mixture with dilute acid gave the equilibrium mixture containing approximately 67% of the 5β isomer.[20] Reaction of ketone **6** with methylenetriphenylphosphorane in Me_2SO gave olefin **7** with the same degree of selectivity observed in the reaction of ketone **9** under similar conditions. This racemic material was identical in its spectral properties with a sample prepared from podocarpic acid (**2**), by removal of the phenolic hydroxyl group,[21] to give acid **4**, which was decarboxylated with lead tetraacetate to give a mixture of olefins.[7a,8] Pure olefin **7** was separated from its isomers by selective epoxidation of the more substituted Δ^3 and Δ^4 olefins.[9]

Some efforts were made to increase the selectivity of the Wittig reaction; however, the best results (86% of olefin **7**, 14% of the apparent 5β isomer) were obtained under the usual conditions for dimsyl ion catalyzed generation of the phosphorus ylide.[4,6] The use of excess sodium hydride gave only recovered ketone, while carrying out the condensation of the ketone with the ylide at room temperature led to a mixture containing only 70% of the desired olefin (**7**).

Although a new synthetic path to the tricyclic nucleus of the diterpenoid acids had been developed, in view of the lack of complete trans selectivity in the Wittig reaction the original plan of using completely synthetic material to synthesize acids **3** and **4** was abandoned. Instead an alternative system was selected for the development of methodology for the introduction of the carboxylic acid group at C-4. The substrate chosen was olefin **10**, an analogue of olefin **7**, but which is readily available in quantity from dehydroabietic acid.[8,22]

The conversion of olefin **10**, via 19-norabieta-8,11,13-trien-18-al (**17**) to 4-epidehydroabietic acid (callitrisic acid, **18**) has been reported by Pelletier,[23] and a similar transformation has been reported by Ziegler.[10] Thus, a method for the introduction of an axial carboxyl group from olefin **10** is available. In an effort to improve this sequence aldehyde **17** was converted to methyl ester **19** by oxidation, followed by esterification. This ester afforded the methyl ester of 4-epidehydroabietic acid (**18**) on treatment with lithium diisopropylamide followed by methyl iodide; however, the yield of isolated product from this sequence was very low (2%) and could not be improved by varying the reaction conditions. An improvement in the published method for converting aldehyde **17** to acid **18** was made when it was found that methylation of aldehyde **17** with potassium triphenylmethide[24] afforded abieta-8,11,13-trien-19-al (**20**) in 91% isolated yield. The oxidation of aldehyde **20** to acid **18** has been reported.[23]

Although the stereoselective conversion of aldehyde **17** to

the axial carboxylic acid is quite routine, the introduction of an equatorial carboxyl group is less straightforward, owing to the stereochemical course of alkylation at C-4 which invariably leads to the introduction of an equatorial alkyl group.[23] A conversion of ketone **6** to either C-4 epimer would appear to be possible using the combination of an elegant, but lengthy, sequence developed recently by Trost[25] with a sequence devised by Wenkert;[26] however, a direct, short, stereoselective conversion of aldehyde **17** to a compound having the correct stereochemistry and functionality at C-4 proved to be feasible. The key step of this sequence was the reduction of a highly sterically hindered aldehyde, such as **20** to the corresponding alkane. That this reduction was feasible was realized when aldehyde **20** was subjected to the Wolff–Kishner reduction to afford abieta-8,11,13-triene (**21**).[27]

The conversion of aldehyde **17** to a 4α-carboxylic acid precursor was accomplished by alkylation with potassium triphenylmethide–allyl bromide to give aldehyde **22** followed by Wolff–Kishner reduction to hydrocarbon **23.** Periodate–permanganate oxidation afforded homodehydroabietic acid **24,** identical in all respects with a sample prepared by homologation of dehydroabietic acid.[3b] This compound has been degraded to dehydroabietic acid **1** by both Stork[3b] and Ireland.[3c] In view of the fact that ketone **9** has been synthesized,[28] the conversion of ketone **9** to acid **24** constitutes a formal total synthesis of dehydroabietic acid.

Experimental Section[29]

18-Norabieta-4(19),8,11,13-tetraene (10). To a solution of 21.28 g (83.77 mmol) of the mixture of olefins obtained by the lead tetraacetate oxidation of dehydroabietic acid[7a,8] in 900 mL of methylene chloride was added 10.47 g (51.6 mmol) of *m*-chloroperbenzoic acid (85%) in 100 mL of methylene chloride. The solution was stirred at room temperature for 0.75 h and excess 10% aqueous sodium iodide was added. The organic layer was drawn off and washed twice with excess 10% aqueous sodium bisulfite and twice with 10% aqueous sodium carbonate. The methylene chloride was dried and evaporated to give 20.28 g of a clear yellow oil. The crude product was taken up in hexane and chromatographed on 1000 g of activity I neutral alumina. Elution with hexane gave 6.98 g (75%) of olefin, the spectral properties of which agreed with those reported previously.[8]

18,19-Dinorabieta-8,11,13-trien-4-one (9). To a solution of 0.19 g (1.20 mmol) of potassium permanganate and 12.12 g (80.0 mmol) of sodium periodate in 350 mL of water was added 13.2 g of potassium carbonate. To this mixture was added 2.00 g (7.87 mmol) of olefin **10** dissolved in 350 mL of *tert*-butyl alcohol and the mixture was stirred for 72 h at room temperature. The mixture was filtered by gravity and the *tert*-butyl alcohol removed on the steam bath at water-pump pressure. The aqueous residue was extracted with ether and the combined ether extracts were dried and evaporated to give a yellow oil. This oil was dissolved in 4:1 hexane–benzene and chromatographed on 70 g of silica gel. Elution with 1:1-benzene–ethyl acetate afforded 0.843 g (42%) of pure *trans* ketone (**9,** 5α-H) as a yellow oil: IR 5.85 μ; NMR δ 0.99 (s, 3 H, C-10 methyl), 1.21 (d, J = 7 Hz, 6 H, isopropyl methyl), 6.90–7.20 (m, 3 H, ArH). Chromatography on alumina afforded the equilibrium mixture containing 67% of the 5β isomer.[7]

Heating a solution of 0.501 g of the 5α ketone in 25 mL of diglyme with 2.5 mL of 2 M hydrochloric acid on the steam bath for 0.5 h gave the same mixture of cis and trans ketones.

Wittig Reaction of 18,19-Dinorabieta-8,11,13-trien-4-one. A. To 0.200 g (4.17 mmol) of sodium hydride (50% dispersion in mineral oil), which had been washed repeatedly with hexane, and which was kept under dry nitrogen, was added 6 mL of freshly distilled dimethyl sulfoxide. The mixture was stirred at 65–72 °C until the sodium hydride had dissolved and cooled to room temperature and a solution of 1.428 g (4.00 mmol) of methyltriphenylphosphonium bromide in 4 mL of dimethyl sulfoxide was added and the mixture stirred for 5 min. A solution of 0.256 g (1.00 mmol) of 18,19-dinorabieta-8,11,13-trien-4-one (**9**) in 4 mL of dimethyl sulfoxide was added and the mixture stirred and heated for 16 h under nitrogen at 62–65 °C. The mixture was cooled to room temperature, poured into water, and extracted with hexane. The hexane extracts were washed with water, dried, and evaporated to give a colorless oil which was dissolved in hexane and chromatographed on 20 g of basic alumina. Elution with hexane afforded 0.080 g (32%) of colorless oil. GLC (OV-17, 235 °C) showed the product to contain 92.5% of the 4(19) olefin (**10**) and 7.5% of another compound, presumably the 5β olefin.

B. When 0.323 g (6.73 mmol) of sodium hydride as a 50% oil dispersion was reacted as described above with 10 mL of dimethyl sulfoxide, 2.285 g (6.40 mmol) of methyltriphenylphosphonium bromide in 8 mL of dimethyl sulfoxide, and 0.410 g (1.60 mmol) of the equilibrium mixture of ketones **9** in 8 mL of dimethyl sulfoxide, 0.120 g (30%) of a colorless oil was obtained after chromatography. GLC (OV-17, 235 °C) showed the product to contain 89% of the 5α olefin (**10**) and 11% of the 5β isomer.

18-Norabieta-8,11,13-triene (11). A solution of 0.038 g of 18-norabieta-4(19),8,11,13-tetraene (**10**) from the Wittig reaction in 15 mL of 95% ethanol was hydrogenated at 50 psig using Adams' catalyst. The catalyst was filtered off using Celite and the solvent evaporated to give 0.033 g (86%) of hydrocarbon **11** as a colorless oil. The product had identical spectral data with those of a sample prepared earlier.[8]

Cyclizations of 2-(2-Phenylethyl)cyclohexane-1,3-dione. A. To 100.0 g of polyphosphoric acid at 120 °C was added with stirring 7.793 g of crude, crystalline 2-(2-phenylethyl)cyclohexane-1,3-dione.[12] The temperature was increased at 160 °C and the mixture stirred at that temperature for 0.75 h. After cooling to 90 °C, the mixture was poured into water, cooled, and extracted with ether. The ether extracts were combined, washed with water, dried, and evaporated to give 5.039 g of dark yellow oil. The crude product was dissolved in hexane and chromatographed on Camag activity I acid-washed alumina. Elution with 1:1 hexane–benzene gave 1.495 g of 1,2,3,4-tetrahydrophenanthrene **13,** as a colorless oil which was identical with an authentic sample. Repeated rechromatography using Woelm activity I neutral alumina and elution with benzene gave 0.034 g of 1,2,3,4-tetrahydro-1-ketophenanthrene **12,** which was identical with an authentic sample. Further elution with benzene gave a yellow oil which crystallized on standing. Recrystallization from 30–60 °C petroleum ether gave 0.400 g of 1,2,3,4,9,10-hexahydro-1-ketophenanthrene (**5**), mp 48–48.5 °C (lit. 48–49 °C[12]) as light yellow plates: IR 6.00 μ; NMR δ 1.78–3.45 (m, 10 H, aliphatic H), 7.15–7.85 (m, 4 H, ArH); UV 288 nm (log ε 4.12), 235 (4.13), 298 (4.12). The 2,4-dinitrophenylhydrazone had mp 260–262 °C (lit. 262–263 °C[12]). Rechromatography and elution with benzene afforded 0.070 g of 1,2,3,9,10,10a-hexahydro-3-ketophenanthrene (**14**), which was identical with the material described below.

In another reaction, 0.150 g of crude, crystalline 2-(2-phenylethylcyclohexane)-1,3-dione was heated in 15.0 g of polyphosphoric acid in the manner described above to give 0.110 g of brown oil. The crude product was dissolved in hexane and chromatographed on 8.0 g of Camag activity I acid-washed alumina. Elution with 2:1 hexane–benzene gave 0.022 g of phenanthrene which was twice sublimed (80 °C, 0.025 mm) to give white crystals, mp 94–97 °C, mixture melting point with a commercial sample 97.5–99 °C.

B. In a typical analytical run in which the products were not isolated, 0.50 g of unrecrystallized diketone was added with stirring to 30 g of polyphosphoric acid at 120 °C. The mixture was stirred at 160 °C for 0.75 h. After cooling to 80 °C, the reaction mixture was poured into water, cooled, and extracted with ether. The combined ether extracts were washed with water, dried, and evaporated to give a brown oil. GLC of the crude product (SE-30, 210 °C) showed the mixture to contain 5% 1,2,3,4-tetrahydrophenanthrene (**13**), 4% phenanthrene, 78% 1,2,3,4,9,10-hexahydro-1-ketophenanthrene (**5**), and 14% of a mixture of 1,2,3,4-tetrahydro-1-ketophenanthrene (**12**) and enone **14.**

When this reaction was carried out using 0.150 g of crude, crystalline diketone in 15 g of polyphosphoric acid, the reaction mixture contained 42% tetrahydrophenanthrene (**13**), 21% phenanthrene, 29% of enone **5,** and 8% of ketone **12.**

C. For the preparation of quantities of enone **5,** the cyclization of recrystallized (mp 149–151 °C) 2-(2-phenylethyl)cyclohexane-1,3-dione was carried out as described above. From 15.0 g of diketone in 2500 g of polyphosphoric acid there was obtained 13.8 g of crude enone as a dark brown oil. GLC (SE-30, 210 °C) indicated that this material was contaminated with ca. 5% of the hydride transfer products. Recrystallization from petroleum ether gave 10.6 g (77%) of pale yellow needles of sufficient purity to carry out the succeeding reactions.

1,2,3,4-Tetrahydro-1-phenanthrone (12). This material was prepared by the polyphosphoric acid catalyzed cyclization of 4-(1-naphthyl)butanoic acid,[30] and was obtained as crystals from hexane, mp 96–96.5 °C (lit. 96–97 °C[31]). This material was identical in all respects with the material described above.

1,2,3,4-Tetrahydrophenanthrene (13). This material was prepared by the Wolff–Kishner reduction of the semicarbazone of

1,2,3,4-tetrahydro-1-ketophenanthrene. From 0.414 g of semicarbazone there was obtained 0.309 g (97%) of hydrocarbon **13** as a colorless oil which crystallized on standing in the freezer: NMR δ 1.80 (m, 4 H, H-1 and H-4), 2.82 (m, 4 H, H-2 and H-2), 6.85–7.80 (m, 6 H, ArH); UV 280 nm (log ϵ 3.74), 308 (2.97), 315 (2.76), 325 (2.94). The picrate has mp 109–110 °C (lit. 111 °C[31]), mixture melting point with the picrate from the cyclization of the dione 110–111 °C.

1,2,3,9,10,10a-Hexahydro-3-ketophenanthrene (14). This material was prepared by a modification of the published procedure.[13,19] From 5.00 g of 1-tetralone there was obtained, following condensation with ethyl formate and annelation with methyl vinyl ketone, 0.953 g (14%) of enone **14** as pale yellow crystals from cyclohexane. This material had mp 82–83 °C (Mousseron reports mp 103 °C[13]); mixture melting point with the material described above from the cyclization reaction 80–81 °C; IR 5.99 μ; NMR δ 1.40–3.10 (m, 9 H, aliphatic H), 6.60–6.65 (d, J = 3 Hz, 1 H, H-4), 7.18–7.25 (m, 3 H, ArH), 7.65–7.82 (m, 1 H= H-5); UV 228 nm (log ϵ 3.97), 235 (3.92), 300 (4.25).

Anal. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 85.05; H, 7.28.

3,4-Dihydrophenanthrene (16). A. To a solution of 0.100 g of 1,2,3,4-tetrahydro-1-phenanthrol (**15**)[32] dissolved in 20 mL of toluene was added a catalytic amount of *p*-toluenesulfonic acid. The reaction mixture was heated at reflux for 2.75 h, cooled, washed with water, and dried and the solvent was evaporated leaving 0.075 g of light yellow solid. The crude product was dissolved in hexane and chromatographed on Camag activity I basic alumina. Elution with hexane gave 0.050 g (55%) of clear plates: mp 65–66 °C; IR 6.20 μ; NMR δ 2.45 (m, 2 H, H-4), 3.18 (t, J = 8 Hz, 2 H, H-3), 6.12 (m, 1 H, H-2), 6.55 (q, J = 1 and 6 Hz, 1 H, H-1), 7.10–8.15 (m, 6 H, ArH).

Anal. Calcd for $C_{14}H_{12}$: C, 93.33; H, 6.66. Found: C, 93.12; H, 6.56.

B. To 0.198 g of 1,2,3,4-tetrahydro-1-phenanthrol (**15**) in 4 mL of pyridine was slowly added 0.35 mL of phosphoryl chloride. The solution was heated on the steam bath for 1 h, cooled slightly, and poured into water. The aqueous mixture was extracted with ether; the ether extract was washed with cold 10% aqueous hydrochloric acid and water, dried, and evaporated, giving 0.025 g (14%) of light yellow oil. This material was identical with that described in part A above.

3-(2-Carboxy-1-naphthyl)propanoic Acid. To a solution of 0.012 g (0.07 mmol) of potassium permanganate, 1.70 g (7.94 mmol) of sodium periodate, and 1.75 g of potassium carbonate dissolved in 40 mL of water was added 0.144 g (0.80 mmol) of 3,4-dihydrophenanthrene dissolved in 40 mL of *tert*-butyl alcohol, the reaction mixture was stirred for 20 h at room temperature, the *tert*-butyl alcohol was removed on the steam bath at water pump pressure, and the aqueous residue was acidified with 10% aqueous sulfuric acid and extracted with ether. The ether solution was extracted with 2.5% aqueous potassium hydroxide and the combined alkaline extracts were washed with ether and acidified with 10% aqueous hydrochloric acid. The product was isolated by extraction. Recrystallization from ether/petroleum ether gave 0.083 g (42%) of white needles, mp 202–203 °C (lit. 203 °C[18]), mixture melting point with material prepared by the method of Meyer[18b] 203 °C.

4a-Methyl-1,2,3,4,4a,9,10,10a-octahydro-1-ketophenanthrene (6). To a rapidly stirred mixture of 23.05 g (121.0 mmol) of cuprous iodide and 165 mL of anhydrous ether in a Morton flask at 0 °C under nitrogen was slowly added 198 mL (256.4 mmol) of methyllithium (1.30 M in ether). The mixture was stirred for 5 min and 6.00 g (30.3 mmol) of 1,2,3,4,9,10-hexahydro-1-ketophenanthrene (**5**) in 165 mL of anhydrous ether was slowly added. The yellow, heterogeneous mixture was stirred at 0 °C for 2 h. The mixture was slowly poured into a rapidly stirred solution of cold 1.2 M hydrochloric acid and the resulting mixture was repeatedly extracted with ether. The combined ether extracts were washed twice with 10% aqueous sodium bisulfite and once with saturated aqueous sodium chloride, dried, and evaporated to give 6.067 g of brown oil. The oil was dissolved in benzene and chromatographed on 300 g of Woelm activity I silica gel. Elution with 100:1 benzene–ethyl acetate gave 2.861 g (44%) of yellow oil. By comparison of NMR peak heights, the product was found to contain 12% of 5α ketone and 88% of the 5β isomer.

A solution of 0.545 g of this ketone mixture in 26 mL of diglyme containing 2.5 mL of 2 M hydrochloric acid was heated on the steam bath for 0.5 h. The mixture was diluted with water, cooled, and extracted several times with hexane. The combined hexane extracts were washed several times with water, dried, and evaporated to give a yellow oil. The oil was dissolved in 1:1 hexane–benzene and filtered through 25 g of activity I silica gel. Elution with 2:1 benzene–ethyl acetate afforded 0.365 g (67%) of ketone mixture as a yellow oil. By NMR integration the mixture was found to contain 34% of the 5α isomer and 66% of the 5β compound: IR 5.85 μ; NMR, trans isomer, δ 1.00 (s, 3 H, C-10 methyl); cis osimer, δ 1.24 (s, 3 H, C-10). These properties agree with those reported by Stork and Burgstahler.[28]

19-Norpodocarpa-4(18),8,11,13-tetraene (4aβ-Methyl-1-methylene-1,2,3,4,4a,9,10,10aα-octahydrophenanthrene, 7). A. To 0.3472 g (7.23 mmol) of sodium hydride (50% oil dispersion which had been repeatedly washed with hexane and maintained in a helium atmosphere was added 10 mL of dimethyl sulfoxide, freshly distilled from calcium hydride, and the mixture was stirred at 65–72 °C until solution occurred. The flask was cooled to room temperature and a solution of 2.295 g (6.43 mmol) of methyltriphenylphosphonium bromide in 8 mL of dimethyl sulfoxide was added. The mixture was sitrred for 5 min and a solution of 0.344 g (1.61 mmol) of 4a-methyl-1,2,3,4,4a,9,10,10a-octahydro-1-ketophenanthrene (**6**) in 5 mL of dimethyl sulfoxide was added. The mixture was cooled to room temperature, poured into water, and extracted with ether. The ethereal solution was washed with water, dried, and evaporated to give a light yellow oil. The oil was taken up in hexane and filtered through 20 g of Camag activity I basic alumina. Elution with hexane gave 0.140 g (41%) of colorless oil which contained 86% of the 5α olefin and had an identical infrared spectrum with that of the material described in B below.

B. To a solution of 1.00 g (3.88 mmol) of podocarpa-8,11,13-trien-19-oic acid[21] dissolved in 15 mL of dry benzene and 1 mL of dry pyridine was added 2.00 g (4.51 mmol) of lead tetraacetate. The mixture was stirred for 1 h at room temperature, then for 3 h at reflux, cooled, filtered through Celite, and washed several times with benzene. The filtrate and washings were combined and concentrated. The resulting yellow oil was dissolved in hexane, washed twice with dilute hydrochloric acid and twice with water, and dried and the hexane evaporated. The product was taken up in hexane and filtered through 30 g of acid-washed alumina to give 0.717 g (87%) of clear, colorless oil which contained 34% 19-norpodocarpa-4(18),8,13-tetraene (**7**) and 66% of a mixture of 19-norpodocarpa-4,8,11,13-tetraene plus 19-norpodocarpa-3,8,11,13-tetraene (analysis by NMR). To a solution of this olefin mixture in 53 mL of methylene chloride was added 0.502 g (2.47 mmol) of *m*-chloroperbenzoic acid (85%) and the mixture was stirred at room temperature for 0.75 h. Excess 10% aqueous sodium iodide was added, and the organic layer drawn off and washed twice with excess 10% aqueous sodium bisulfite and twice with 10% aqueous sodium carbonate. The methylene chloride was dried and evaporated to give 0.637 g of colorless oil. The crude product was taken up in hexane and chromatographed on 32 g of Camag activity I basic alumina. Elution with hexane gave 0.134 g (57%) of clear oil: IR 6.09 μ; NMR δ 1.02 (s, 3 H, C-10 methyl), 4.70–4.95 (m, 2 H, CCH_2), 7.10–7.50 (m, 4 H, ArH). The infrared and NMR spectra were identical with those of the racemate described in part A.

Anal. Calcd for $C_{16}H_{20}$: C, 90.51; H, 9.49. Found: C, 90.68; H, 9.54.

Methyl 19-Norabieta-8,11,13-trien-18-oate (19). To a stirred solution of 5.70 g (21.11 mmol) of 19-norabieta-8,11,13-trien-18-al (**17**) prepared by the method of Pelletier[23] in 285 mL of acetone at room temperature was added dropwise 12 mL (24.0 mmol) of Jones reagent over a 1-min period. After 20 min, 8 mL of methanol was added, and the mixture was diluted with brine and extracted with ether. The ether extracts were combined, dried, and evaporated to give a yellow oil. The crude acid was dissolved in 10% aqueous potassium hydroxide, washed twice with ether, and precipitated with dilute sulfuric acid. The precipitate was taken up in ether and the ether was dried and evaporated to give 3.28 g (54%) of acid as a yellow foam: IR 5.85 μ; NMR δ 1.11 (s, 3 H, C-10 methyl), 6.85–7.25 (m, 3 H, ArH), 10.37 (s, 1 H, COOH).

A solution of 3.43 g (12.00 mmol) of this material in methylene chloride was treated with an excess of ethereal diazomethane. The solvent was removed under vacuum to give 3.466 g of crude ester as a yellow solid. Recrystallization from methanol gave 2.87 g (80%) of white needles: mp 88–89 °C; IR 5.72 μ; NMR δ 1.10 (s, 3 H, C-10 methyl), 1.23 (d, J = 7 Hz, isopropyl methyl), 3.68 (s, 3 H, $COOCH_3$), 6.82–7.30 (m, 3 H, ArH).

Anal. Calcd for $C_{20}H_{28}O_2$: C, 79.96; H, 9.39. Found: C, 80.14; H, 9.40.

Methyl Abieta-8,11,13-trien-19-oate. To a flame-dried flask at 0 °C under helium was added 0.460 g (4.55 mmol) of diisopropylamine and then dropwise, over a 4-min period, 2.1 mL (4.55 mmol) of 2.2 M *n*-butyllithium. After stirring at 0 °C for 0.25 h, the lithium diisopropylamide precipitated as a white solid. A cold solution of one crystal of triphenylmethane in 3 mL of hexamethylphosphoramide, freshly distilled from calcium hydride, was added and to the resulting bright red solution was added a solution of 0.667 g (2.22 mol) of methyl 19-norabieta-8,11,13-trien-18-oate (**19**) in 4 mL of hexamethyl-

phosphoramide. The reaction mixture remained bright red after stirring for 1 h at 0 °C. To the cold mixture was then added 4.72 g (33.24 mmol) of methyl iodide in one portion. The mixture was stirred and heated at 40 °C for 2 h and cooled to room temperature and 12 mL of petroleum ether was added. Sufficient 10% aqueous hydrochloric acid was added until the mixture became acidic and the aqueous layer was then drawn off and twice extracted with petroleum ether. The organic layers were combined and washed repeatedly with 10-mL portions of 10% aqueous hydrochloric acid, water, and saturated brine. The solvent was dried and evaporated to give 0.416 g of light yellow foam. The product was dissolved in 6:1 hexane–benzene and chromatographed on 20 g of activity I acid-washed alumina. Elution with 5:1 hexane–benzene afforded 0.014 g (2%) of oil which crystallized on the addition of methanol; recrystallization from methanol gave white crystals, mp 78–78.5 °C (lit.[33] 79–80 °C), mmp 74.5–77 °C. The infrared spectrum was identical with that of an authentic sample.

Abieta-8,11,13-trien-19-al (20). To 1.13 g of potassium hydride (6.75 mmol, 24% oil dispersion), which had been thoroughly washed with dry hexane and anhydrous ether and which was maintained in an atmosphere of helium, was added 3 drops of dry dimethyl sulfoxide. Following the cessation of the evolution of hydrogen, a solution of 1.647 g (6.75 mmol) of triphenylmethane in 6.5 mL of dimethyoxyethane (freshly distilled from lithium aluminum hydride) was added and the mixture stirred for 0.25 h at 40 °C. The tritylpotassium was added slowly to a solution of 0.450 g (1.66 mmol) of 19-norabieta-8,11,13-trien-18-al (**17**) dissolved in 2.0 mL of dimethoxyethane under helium until a permanent red color was obtained. The mixture was stirred for 10 min and 2.5 mL of methyl iodide was added all at once, with the immediate discharge of the red color and the formation of a precipitate. The heterogeneous mixture was stirred overnight at room temperature; the reaction mixture was poured into cold water and acidified with concentrated hydrochloric acid and the product extracted with several portions of ether. The etheral extracts were combined, washed thoroughly with water, and dried and the solvent was evaporated to give a mixture of a yellow oil and a solid. The product was taken up in hexane and chromatographed on 50 g of silica gel. Elution with benzene gave 0.433 g (91%) of a light yellow oil: IR 3.65, 5.82 μ; NMR δ 1.08 (s, 3 H, C-18 methyl), 1.11 (s, 3 H, C-10 methyl), 1.28 (d, J = 7 Hz, 6 H, isopropyl methyl), 7.15–7.46 (m, 3 H, ArH), 10.20 (d, J = 1 Hz, CHO). These spectral properties agree with those reported by Pelletier.[23]

Abieta-8,11,13-triene (21). To the semicarbazone from 0.433 g (1.52 mmol) of abieta-8,11,13-trien-19-al (**20**) was added a solution of 3.66 g of potassium hydroxide in 25 mL of diethylene glycol and enough water to effect solution. The mixture was distilled until a temperature of 185 °C was reached and then heated at reflux for 5 h. The reaction mixture was cooled to 90 °C, poured into water, and extracted several times with hexane. The combined hexane extracts were washed with water, dried, and evaporated to give a yellow oil. The oil was taken up in hexane and chromatographed on 50 g of acid-washed alumina. Elution with hexane gave 0.129 g (31%) of a clear, colorless oil which crystallized on standing in the freezer. The oil had identical spectral properties with those reported.[27]

18-Dihomoabieta-8,11,13,18a-tetraen-19-al (22). A solution of tritylpotassium prepared as described above was added slowly to a solution of 0.981 g (3.63 mmol) of 19-norabieta-8,11,13-trien-18-al (**17**) dissolved in 2.0 mL of dimethoxyethane under helium until a permanent red color was obtained. The mixture was stirred for 10 min and 3.0 mL of allyl bromide was added all at once, with the immediate discharge of the red color and the formation of a precipitate. The mixture was stirred at room temperature overnight, poured into cold water, and acidified with concentrated hydrochloric acid and the product was extracted with several portions of ether. The ethereal extracts were combined, washed thoroughly with water, and dried and the solvent was removed at reduced pressure to give a mixture of a yellow oil and a solid. The product was taken up in hexane and chromatographed on silica gel. Elution with benzene gave 1.078 g (96%) of light yellow oil: IR 3.65, 5.82, 6.10, 6.22 μ; NMR δ 1.05 (s, 3 H, C-10 methyl), 1.25 (d, J = 7 Hz, 6 H, isopropyl methyl), 4.95–6.00 (m, 3 H, C-18a and C-18b, CH=CH_2), 7.00–7.50 (m, 3 H, ArH), 10.00 (s, 1 H, CHO). The 2,4-dinitrophenylhydrazone had mp 192–193 °C.

Anal. Calcd for $C_{28}H_{34}N_4O_4$: C, 68.55; H, 6.99; N, 11.42. Found: C, 68.70; H, 7.10; N, 11.24.

18-Dihomoabieta-8,11,13,18a-tetraene (23). To a solution of 1.063 g (3.43 mmol) of 18-dihomoabieta-8,11,13,18a-tetraen-19-al dissolved in 40 mL of diethylene glycol was added 3.0 mL of 99% hydrazine and the mixture was heated at reflux for 1 h. The mixture was cooled and a solution of 3.0 g of potassium hydroxide in 15 mL of diethylene glycol and enough water to effect solution was added. The mixture was distilled until a temperature of 185 °C was reached and then heated at reflux for 4.5 h, cooled, poured into water, and extracted several times with hexane. The combined hexane extracts were washed with water, dried, and evaporated to give a yellow oil. The oil was taken up in hexane and chromatographed on 50 g of Camag activity I basic alumina. Elution with hexane afforded 0.537 g (53%) of clear, colorless oil: IR 6.10, 6.20 μ; NMR δ 0.92 (s, 3 H, C-10 methyl), 1.20 (s, 3 H, C-19 methyl), 2.22 (d, J = 7 Hz, 6 H, isopropyl methyl), 2.62–2.97 (m, 2 H, C-18 CH_2), 4.72–5.75 (m, 3 H, C-18a and C-18b CH=CH_2), 6.72–7.70 (m, 3 H, ArH).

Anal. Calcd for $C_{22}H_{32}$: C, 89.12; H, 10.88. Found: C, 89.33; H, 10.92.

18-Homo-8,11,13-trien-18a-oic Acid (Homodehydroabietic Acid, 24). To a solution of 0.325 g (1.10 mmol) of 18-dihomoabieta-8,11,13,18a-tetraene (**23**) in 50 mL of *tert*-butyl alcohol was added a solution of 0.045 g of potassium permanganate, 2.59 g of sodium periodate, and 1.98 g of potassium carbonate in 50 mL of water. The reaction mixture was stirred at room temperature for 22 h and filtered and the solvent removed at water-pump pressure. The aqueous residue was acidified with 10% sulfuric acid and the product extracted with 1:1 hexane–ether. The combined organic extracts were washed with 10% aqueous potassium hydroxide. The basic extract was acidified with concentrated hydrochloric acid and extracted with ether. The ether extract was washed with water, dried, and evaporated to give a colorless oil which was twice recrystallized from aqueous methanol to give 0.095 g (28%) of white needles, mp 142–144 °C, mixture melting point with material prepared by Stork's method[3b] 143–144 °C. The infrared spectra of samples prepared by both procedures were identical.

Registry No.—**1**, 6980-63-8; **2**, 15292-90-7; **4**, 10178-11-7; **5**, 62264-34-0; 5αH-**6**, 54170-97-7; 5βH-**6**, 62318-99-4; **7**, 62319-00-0; 5αH-**9**, 62319-01-1; 5βH-**9**, 62319-02-2; 5αH-**10**, 62319-03-3; 5βH-**10**, 62319-04-4; **12** semicarbazone, 62264-35-1; **13**, 1013-08-7; **14**, 53023-33-9; **15**, 62264-36-2; **16**, 38399-10-9; **17**, 62319-05-5; **19**, 62264-37-3; **19** free acid, 62264-38-4; **20**, 62319-06-6; **22**, 62288-64-6; **22** hydrazone, 62264-39-5; **23**, 62264-40-8; 2-(2-phenylethyl)cyclohexane-1,3-dione, 62264-41-9.

References and Notes

(1) Presented at the Southeastern–Southwestern Regional Meeting of the American Chemical Society, Oct 29–31, 1975.
(2) Tennessee Eastman Fellow, 1973–1974.
(3) (a) N. A. Rogers and J. A. Barltrop, *Q. Rev., Chem. Soc.*, **16**, 117 (1962), summarize the earlier synthetic efforts in this area; (b) G. Stork and J. W. Schulenberg, *J. Am. Chem. Soc.*, **84**, 284 (1962); (c) R. E. Ireland and R. C. Kierstead, *J. Org. Chem.*, **31**, 2543 (1966); (d) F. Giarusso and R. E. Ireland, *ibid.*, **33**, 3560 (1968); (e) E. Wenkert, A. Afonso, J. B-son Bredenberg, C. Kaneko, and A. Tahara, *J. Am. Chem. Soc.*, **86**, 2038 (1964); (f) T. A. Spencer, T. D. Weaver, and W. J. Greco, Jr., *J. Org. Chem.*, **30**, 3333 (1965); (g) T. A. Spencer, T. D. Weaver, R. M. Villarica, R. J. Friary, J. Posler, and M. A. Schwartz, *ibid.*, **33**, 712 (1968); (h) T. A. Spencer, R. J. Friary, W. W. Schmiegel, J. F. Simeone, and D. S. Watt, *ibid.*, **33**, 719 (1968); (i) W. L. Meyer and C. W. Sigel, *Tetrahedron Lett.*, 2485 (1967); (j) M. E. Kuehne and J. A. Nelson, *J. Org. Chem.*, **35**, 161 (1970).
(4) J. W. Huffman and M. L. Mole, *J. Org. Chem.*, **37**, 13 (1972).
(5) E. Wenkert and B. G. Jackson, *J. Am. Chem. Soc.*, **80**, 217 (1958).
(6) (a) J. A. Marshall, M. T. Pike, and R. D. Carroll, *J. Org. Chem.*, **31**, 2933 (1966); (b) M. D. Soffer and L. A. Burke, *Tetrahedron Lett.*, 211 (1970).
(7) (a) J. W. Huffman and P. G. Arapakos, *J. Org. Chem.*, **30**, 1604 (1965); (b) J. W. Huffman and R. F. Stockel, *ibid.*, **28**, 506 (1963); (c) J. J. Zeiss and W. B. Martin, *J. Am. Chem. Soc.*, **75**, 5935 (1953); (d) A. Brossi, J. Gutman, and O. Jegar, *Helv. Chim. Acta*, **33**, 1730 (1950); (e) R. P. Jacobsen, *J. Am. Chem. Soc.*, **75**, 4709 (1953).
(8) J. W. Huffman, *J. Org. Chem.*, **35**, 478 (1970).
(9) R. C. Cambie and W. A. Denny, *Aust. J. Chem.*, **22**, 1699 (1969), carried out a similar selective epoxidation reaction in the podocarpic acid series.
(10) F. E. Ziegler and J. A. Kloek, *Tetrahedron Lett.*, 315 (1974).
(11) H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966).
(12) A. J. Birch and H Smith, *J. Chem. Soc.*, 1882 (1951).
(13) M. Mousseron, H. Christol, and R. Salli, *C. R. Acad. Sci.*, **245**, 1366 (1951).
(14) The 2-(2-phenylethyl)cyclohexane-1,3-dione was prepared by the potassium amide catalyzed alkylation of dehydroresorcinol dimethyl ether.[12] The presence of a small quantity of the 4 isomer under these conditions is not unexpected.
(15) J. W. Cook, E. C. Dodds, and W. Lawson, *Proc. R. Soc., London, Ser. B*, **121**, 133 (1937).
(16) C. Reid, *J. Mol. Spectrosc.*, **1**, 18 (1957).
(17) L. A. Paquette, M. J. Kukla, and F. C. Stowell, *J. Am. Chem. Soc.*, **94**, 4920 (1972).
(18) (a) J. S. Bardhan, D. Nasipuri, and R. N. Adhya, *J. Chem. Soc.*, 355 (1956); (b) K. Meyer and R. Reichstein, *Pharm. Acta Helv.*, **19**, 128 (1944); *Chem. Abstr.*, **39**, 516 (1945).

(19) A complete summary of this investigation, with full experimental details, is found in the Ph.D. dissertation of P. G. Harris, Clemson University, 1977.
(20) The position of this equilibrium is the same as that reported by Ziegler (ref 10) for a very similar ketone.
(21) R. C. Cambie, K. P. Mathai, and A. W. Misseu, *Aust. J. Chem.*, **25**, 1253 (1972).
(22) The use of olefin **7**, prepared from podocarpic acid, was briefly considered, but rejected on two grounds. First, podocarpic acid is relatively costly and difficult to obtain in quantity, and second, the preparation of acid **4**, the precursor of olefin **7**, is a multistep sequence, with a mediocre overall yield.
(23) S. W. Pelletier and D. C. Herald, *Chem. Commun.*, 10 (1971).
(24) J. W. Huffman and P. G. Harris, *Synth. Commun.*, **7**, 137 (1977).
(25) B. M. Trost and M. Preckel, *J. Am. Chem. Soc.*, **95**, 7862 (1973). This procedure also leads to the conversion of ketones of the type of **6** and **9** to the 4β-carboxylic acids.
(26) J. P. Tresco, J. L. Fourrey, J. Polonsky, and E. Wenkert, *Tetrahedron Lett.*, 895 (1973).
(27) M. Kitadani, A. Yoshikoshi, Y. Kitahara, J. Campello, J. D. McChesney, D. J. Watts, and E. Wenkert, *Chem. Pharm. Bull.*, **18**, 402 (1970).
(28) G. Stork and A. Burgstahler, *J. Am. Chem. Soc.*, **73**, 3544 (1951).
(29) All melting points were determined on a Kofler hot stage and are uncorrected. Infrared spectra were taken as potassium bromide disks or liquid films on sodium chloride plates, using a Perkin-Elmer Model 137 spectrophotometer, and are reported in microns. Ultraviolet spectra were taken in 95% ethanol (unless otherwise stated), using a Perkin-Elmer Model 202 spectrophotometer, and are reported as λ_{max} in nanometers (log ϵ). Nuclear magnetic resonance spectra were obtained on either a Varian Associates A-60 or a Perkin-Elmer Hitachi Model R-24 nuclear magnetic resonance spectrometer using deuteriochloroform as a solvent and are reported in parts per million relative to tetramethylsilane (δ). Gas–liquid chromatography was carried out on an F and M Model 810 analytical gas chromatograph using a hydrogen flame detector with helium as the carrier gas. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.
(30) W. E. Bachmann and N. L. Wendler, *J. Am. Chem. Soc.*, **68**, 2580 (1946).
(31) G. H. Schroeter, H. Muller, and J. Y. S. Huang, *Ber.*, **62**, 645 (1929).
(32) This alcohol was prepared by the sodium borohydride reduction of ketone **12**. The physical properties were in agreement with those reported in ref 15.
(33) J. W. Huffman, *J. Org. Chem.*, **35**, 3154 (1970).

Synthesis of 2-Alkylcyclopentenones. Jasmone, Dihydrojasmone, and a Prostaglandin Precursor

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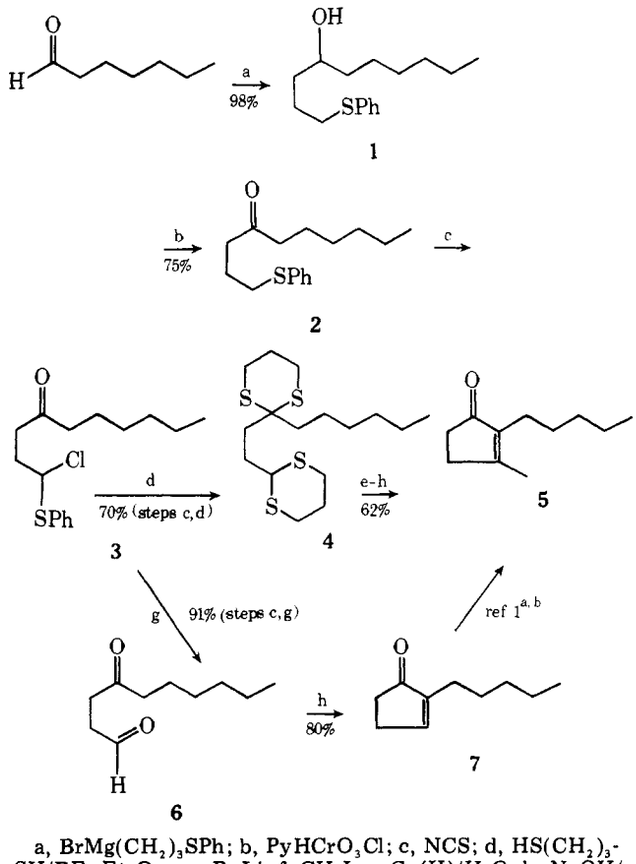
Jasmone (**15**), dihydrojasmone (**5**), and 2-(6-carboxyhexyl)cyclopent-2-en-1-one (**10**) were prepared in several steps from acyclic precursors. Thus, levulinic acid was transformed into a sulfide which was oxidized with *N*-chlorosuccinimide and hydrolyzed to the diketo aldehyde **13**. A chemoselective Wittig reaction, followed by base-catalyzed cyclization, gave jasmone (**15**). Similarly, **5** was prepared from heptanal, while **10** was prepared from azelaic acid monomethyl ester.

2-Alkylcyclopentenones are important intermediates in the preparation of natural products such as jasmones,[1] prostaglandins,[2] steroids,[3] and triterpenes.[4] One method of preparing such compounds is the base-catalyzed cyclization[5] of 1,4-dicarbonyl[6] compounds. While there are many methods of preparing 1,4-diketones,[6a] there are relatively few methods for preparing γ-keto aldehydes.[6b,c] We would like to report a simple sequence of reactions, from readily available starting materials, that permits the synthesis of the 1,4-dicarbonyl precursors of the title compounds.

Grignard reagents prepared from β-halo acetals are known to be unstable,[7] although they have been used for the preparation of alcohols[8] and ketones.[6b] Grignard and lithium reagents prepared from protected bromopropanols and butanols are useful for the preparation of alcohols, ketones, functional homologations, and 1,4-additions to unsaturated systems.[9] However, the preparation of both of these reagents by inexperienced workers is not easy, and the latter reagents are prepared from expensive starting materials. Recently, we showed that Grignard reagents prepared from bromoalkyl phenyl sulfides (easily prepared from the readily available dibromo alkanes) can be used for functional homologations.[10] In this report we present our results on the application of these compounds to the preparation of carbonyl compounds.

While the two sequences outlined in Scheme I for the preparation of dihydrojasmone are longer than the best present method,[11] they illustrate some of the potential of the $PhS(CH_2)_nMgBr$ reagents. Hydroxy sulfide **1**, prepared from heptanal in near-quantitative yields, was oxidized selectively to the carbonyl compound **2** with pyridinium chlorochromate.[12] The key intermediate **3**, prepared by oxidation of **2** with *N*-chlorosuccinimide,[10,13] was transformed into the dithiane **4** and then, by the usual methods[14] of alkylation, hydrolysis, and cyclization, into dihydrojasmone (**5**). Alter-

Scheme I



a, $BrMg(CH_2)_3SPh$; b, $PyHCrO_3Cl$; c, NCS; d, $HS(CH_2)_3SH/BF_3 \cdot Et_2O$; e, *n*-BuLi; f, CH_3I; g, Cu(II)/H_2O; h, NaOH/H_2O/Δ.